REMARKS

Status of the Claims

Claims 1-14, and 21-23 are currently pending in the application. Claims 1-20 stand rejected. Claims 1, 3-6, 8 and 11-14 have been amended as set forth herein. Claims 15-20 have been cancelled herein. All amendments and cancellations are made without prejudice or disclaimer. New claims 21-23 have been added herein. No new matter has been added by way of the present amendments.

Specifically, the amendment to claim 1 is supported by the specification at page 7.

The amendment to claims 3 and 4 are merely clarifying amendments and do not narrow the encompassed subject matter.

Claims 5, 6, 8, 11 and 12 have been amended to depend from claim 1.

Claims 13 and 14 are supported by the specification at page 6.

New claim 21 is supported by the original claims, for instance, original claim 1.

New claim 22 is supported by the specification at page 6, last paragraph.

New claim 23 is supported by the specification at page 5, last paragraph.

Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Presumably claims 1-20 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaswan, U.S. Patent No. 4,649,047 (hereinafter, "Kaswan") taken with Elzinga et al., *Transplantation*, 47(2): 394-395, 1989 (hereinafter "Elzinga et al."), Broadwell et al., *Science*, 217(4555): 164-166, 1982 (hereinafter "Broadwell et al.") and Elias, U.S. Patent No. 5,807,820

(hereinafter, "Elias"). (*See*, Office Action of June 13, 2006, hereinafter, "Office Action"). Claims 15-20 have been cancelled without prejudice or disclaimer, thus obviating the rejection as to these claims. Applicants traverse the rejection as to the remaining claims as hereinafter set forth.

The Examiner is respectfully reminded that M.P.E.P. § 706.02(j) sets forth the standard for establishing a *prima facie* case of obviousness as follows:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

The Examiner admits that Kaswan do not disclose or suggest the following limitations:

a) methods for administering a cyclosporin and DMSO solution by injection into the cerebrospinal fluid, intra-ocular, intravestibular, into or adjacent to the brain or spinal cord, or intravenous, intra-arterial, intraparenchymal spaces, or orally, rectally, vaginally, urethrally, bladder cisternally, nasally, intra- and peri-ocularly or dermally to a patient,

b) an article of manufacture comprising packaging material and a pharmaceutical agent wherein said agent comprises DMSO and a cyclosporin formulation,

c) a method for treating Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, HIV neuropathy, Guillain-Barré syndrome, neural transplantation,

neural xenotransplantation, stroke, brain hemorrhage, brain and spine trauma, ionizing radiation, neurotoxicity of vestibular structures, or retinal detachment (claim 11), and

d) a method for inducing systemic immunosuppression in patients of transplantation or autoimmune disease (claim 12).

The Examiner relies on the secondary reference of Elzinga et al. for disclosure or suggestion that oral administration of cyclosporin in a DMSO solution to rats is highly variable and incomplete but that DMSO is able to penetrate most biological membranes with ease.

The Examiner relies on the secondary reference of Broadwell et al. for disclosure or suggestion that DMSO has a morphological effect on the blood-brain barrier of mice using a 15% concentration of DMSO and that other organs were determined to be normal on gross examination at autopsy.

The Examiner relies on the secondary reference of Elias for disclosure or suggestion of pharmaceutical compositions comprising cyclosporin in a concentration of from 0.1% to 50% based on total weight of the composition useful for topical application.

In summary, the Examiner states that taking all of the disclosures of the secondary references into consideration, DMSO is shown as a carrier in pharmaceutical compositions combined with any agent of interest. The Examiner then summarily concludes that the disclosures of the secondary references, if used to modify the methods disclosed or suggested by Kaswan, disclose or suggest all modes of administration recited in the presently pending claims.

It is apparent that many elements and limitations recited in the present claims are entirely missing from any and all of the cited references. Even the Examiner's own admitted failings of

the disclosure of Kaswan are not cured by the disclosures or suggestions of the cited secondary references of Elzinga et al., Broadwell et al. and/or Elias.

For instance, beginning with claim 1, none of the reference disclose or suggest using DMSO in an amount of 75% by weight or greater of a pharmaceutical composition comprising cyclosporin.

Furthermore, none of the cited references disclose or even remotely suggest administering a pharmaceutical composition comprising DMSO and cyclosporin by injection into cerebrospinal fluid or cerebrospinal fluid spaces of a patient, as recited by the method of claim 3, or intravestibularly, as recited in claim 4.

None of the cited references disclose or suggest administering the pharmaceutical composition according to claim 1 by injection intravenously, intra-arterially or intraparenchymally, as recited in claim 5, or inhalationally or nasally, as recited in claim 6.

As to claim 8, the Examiner admits in the Office Action that Kaswan does not disclose this article of manufacture. Furthermore, the additional comments in the Office Action regarding the secondary references fail to provide all of the elements of claim 8. In fact, no further mention is made throughout the Office Action of an article of manufacture as recited in claim 8.

It follows then that since the secondary references fail to cure the defects of the disclosure of Kaswan with respect to claim 1, the references considered either individually or in combination, further fail to disclose a method of treating any and all of the diseases recited in claim 11. No mention is made in any of the references of any of the diseases recited in claim 11.

Regarding claim 12, the Examiner fully admits that Kaswan fails to disclose or suggest a method for inducing systemic immunosuppression in patients of transplantation or autoimmune

disease. In the remaining remarks of the Office Action regarding the secondary references, the Examiner fails to point out where in the disclosures of the secondary references the missing elements of this method are disclosed or suggested. No further mention is made of immunosuppression or treatment thereof throughout the Office Action.

Claims 13 and 14 further limit claim 1 by specifying unit dosage amounts which are also not disclosed in or suggested by any of the disclosures of any of the references.

Thus, the references cited by the Examiner fail to support a *prima facie* case of obviousness with respect to the presently pending and amended claims because the disclosures of the references, either considered in combination or separately, fail to disclose or suggest each and every limitation of the presently pending claims, as is required. (*See*, *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991)).

Reconsideration and withdrawal of the obviousness rejection of claims 1-14 and 20 are respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 2 and 13-20 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description/new matter requirement. (*See*, Office Action, at page 8). Claims 15-20 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection as to claims 15-20. The Examiner states that the phrase "not intended for ophthalmic, cutaneous, oral or gavage application" is not supported in the original specification. (*Id.*). The Examiner's contention is inconsistent with the disclosure of the specification, legal precedent and the M.P.E.P. (*See*, page 5 of the present specification, and M.P.E.P. at § 2173.05(i), citing

In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977), and *Ex parte Grasselli*, 231 U.S.P.Q. 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984)). Nevertheless, claims 1 and 2 have been amended herein to remove the phrase upon which the rejection is based, thus obviating the rejection.

ENTRY OF AMENDMENTS

The amendments to the claims and new claims should be entered by the Examiner because the amendments and new claims are supported by the as-filed specification and do not add any new matter to the application. Additionally, the amendments and new claims should be entered since they comply with requirements as to form, and place the application in condition for allowance. Further, the amendments and new claims do not raise new issues or require a further search since the amendments incorporate elements from dependent claims into independent claims and/or are supported by the as-filed specification. Finally, if the Examiner determines that the amendments do not place the application in condition for allowance, entry is respectfully requested since they certainly remove issues for appeal.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

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